

08/905046

21jun00 11:24:57 User219783 Session D1599.1

SYSTEM:OS - DIALOG OneSearch

File 65:Inside Conferences 1993-2000/Jun W3

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File 129:PHIND(Archival) 1980-2000/Jun W2

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File 113:European R&D Database 1997

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File 130:PHIND(Daily & Current) 2000/Jun 21

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File 156:Toxline(R) 1965-2000/May

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File 357:Derwent Biotechnology Abs 1982-2000/Jun B2

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File 440:Current Contents Search(R) 1990-2000/Jul W1

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File 144:Pascal 1973-2000/Jun W3

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*File 144: This file is updating weekly now.

File 151:HealthSTAR 1975-2000/Jul

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*File 151: HealthSTAR has been reloaded. Accession numbers have changed

File 348:European Patents 1978-2000/Jun W03

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*File 348: ** NEW FEATURE ** English language translations of French and German abstracts now searchable. See HELP NEWS 348 for info.

File 35:DISSERTATION ABSTRACTS ONLINE 1861-1999/DEC

(c) 2000 UMI

File 77:Conference Papers Index 1973-2000/May

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File 98:General Sci Abs/Full-Text 1984-2000/May

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Set Items Description

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? ds; t 5/3,ab/1--18

- key terms

Set	Items	Description
S1	768	((COLONIZ? OR COLONIS?) (W) FACTOR OR CFA) (3N) (1 OR I) OR CF-AI OR CFA1
S2	4225	CS4 OR (COLI(W) SURFACE OR CS) (3N) 4
S3	64	S1 AND S2
S4	29	S3 AND (MOAB? ? OR MAB? ? OR MONOCLON? OR HYBRIDOM? OR 961-09FE? OR 96(W) (109FE? OR 109(W) (FE8 OR FE(W) 8)) OR 12163 OR H-B12163)
S5	18	RD (unique items)

>>>No range suffix in item list

? t 5/3,ab/1-18

Searcher : Shears 308-4994

>>>No matching display code(s) found in file(s): 65, 113, 129, 130

5/3,AB/1 (Item 1 from file: 156)

DIALOG(R)File 156:Toxline(R)

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03347552 Subfile: BIOSIS-98-32846

Epidemiology and properties of heat-stable enterotoxin-producing *Escherichia coli* serotype O169:H41.

NISHIKAWA Y; HELANDER A; OGASAWARA J; MOYER NP; HANAOKA M; HASE A; YASUKAWA A

Dep. Epidemiol., Osaka City Inst. Public Health Environ. Sci., Tojo-cho, Tennoji, Osaka 543-0026, Japan.

Source: EPIDEMIOLOGY AND INFECTION; 121 (1). 1998. 31-42. Coden: EPINE
Language: ENGLISH

BIOSIS COPYRIGHT: BIOL ABS. Enterotoxigenic *Escherichia coli* (ETEC) serotype O169:H41 organisms have become the most prevalent ETEC in Japan since the first outbreak in 1991. It was assumed that the outbreaks were due to clonal spread of this new ETEC serotype. The relationship of 32 strains isolated from 6 outbreaks were examined for biotype, antibiotic susceptibility, enterotoxigenicity, protein banding pattern, lipopolysaccharide banding pattern, plasmid analysis, and ribotyping. Further, the strains were examined by hemagglutination, surface hydrophobicity, and the ability to adhere to HEP-2 cells. The present study suggests that the outbreaks were caused by multiple clones of STp-producing O169:H41 since they showed differences in ribotype and outer membrane protein banding patterns. The strains did not agglutinate human or bovine red blood cells in a mannose-resistant manner. They adhered to HEP-2 cells in a manner resembling enteroaggregative *E. coli*. Five strains were examined by dot-blot tests for the *colonization*** *factor*** antigens *CFA***/*I***, CS1, CS2, CS3, *CS4***, CS5, CS6, CS7, PCF0159, PCF0166 and CFA/III. Although four strains expressed CS6, no structure for CS6 was identified. A strain that the anti-CS6 *MAbs*** did not react with could adhere to HEP-2 cells in mannose resistant manner; thus, it is unlikely that CS6 play an important role in the adhesion to the cells. Electron microscopy studies of the O169:H41 strains suggested that curly fimbriae, a possible new colonization factor, may be playing an important role in the adhesion of the bacteria to HEP-2 cells. In conclusion, outbreaks due to ETEC O169:H41 were caused by multiple clones, and the strains should be examined in detail for a possible new colonization factor.

5/3,AB/2 (Item 2 from file: 156)

DIALOG(R)File 156:Toxline(R)

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03245103 Subfile: BIOSIS-94-34421

*Monoclonal*** antibodies against enterotoxigenic *Escherichia coli* *colonization*** *factor*** antigen *I*** (*CFA***/*I***) that cross-react

Searcher : Shears 308-4994

immunologically with heterologous CFAs.

RUDIN A; MCCONNELL MM; SVENNERHOLM A-M

Dep. Med. Microbiol. Immunol., Univ. Goteborg, Guldhedsgatan 10A, 413 46 Goteborg, SWE.

Source: INFECTION AND IMMUNITY; 62 (10). 1994. 4339-4346. Coden: INFIB

Language: ENGLISH

BIOSIS COPYRIGHT: BIOL ABS. Enterotoxigenic Escherichia coli binds to enterocytes in the small intestine by means of antigenically distinct colonization factors (CFs), usually termed colonization factor antigens (CFAs), coli surface antigens (CS), or putative colonization factor antigens (PCFs). To explore the immunological relationship between different CFs, we dissociated *CFA***/I*** fimbriae into subunits and produced *monoclonal*** antibodies (*Mabs***) against these subunits. We selected three *Mabs*** that cross-reacted immunologically with a number of different, whole purified CFs in a dot blot test and with the corresponding subunits in sodium dodecyl sulfate-polyacrylamide gel electrophoresis. One of the *Mabs***, *i***.e., subunit *CFA***/I*** 17:8 (S-*CFA***/I*** 17:8), reacted more strongly with subunits of *CFA***/I*** than with whole purified fimbriae. This *Mab*** cross-reacted with whole purified fimbriae and subunits of *CS4***, PCF0166, CS1, and CS2. Moreover, it bound strongly to a peptide of 25 amino acids corresponding to the N-terminal end of *CFA***/I***. The other two *Mabs***, *i***.e., S-*CFA***/I*** 5:6 and S-*CFA***/I*** 8:11, cross-reacted with CS1, CS2, *CS4***, PCF0166, and CS17 fimbriae but reacted only slightly or not at all with the *CFA***/I*** peptide. *Mabs*** S-*CFA***/I*** 17:8 and S-*CFA***/I*** 5:6 were shown to inhibit hemagglutination by bacterial strains that express either *CFA***/I***, CS1, or *CS4***. In addition, the binding of enterotoxigenic E. coli strains expressing *CFA***/I***, CS2, *CS4***, and PCF0166 to enterocyte-like cell-line Caco-2 was inhibited by both *Mabs***. These results show that several antigenically different CFs have common epitopes and that among these at least one is located in the N-terminal end of the subunit protein. Moreover, antibodies against the common epitopes seem to block binding of the bacterial strains that express different CFs to both erythrocytes and Caco-2 cells.

5/3,AB/3 (Item 3 from file: 156)

DIALOG(R)File 156:Toxline(R)

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03090909 Subfile: BIOSIS-91-32554

Colonization factors of enterotoxigenic Escherichia coli isolated from children with diarrhea in Argentina.

BINSZTEIN N; JOUVE MJ; VIBOUD GI; MORAL LL; RIVAS M; ORSKOV I; AHREN C; SVENNERHOLM A-M

Instituto Nacional Microbiologia "Carlos G. Malbran", Velez Sarsfield 563, 1281 Buenos Aires, Argentina.

Source: J CLIN MICROBIOL; 29 (9). 1991. 1893-1898. Coden: JCMID

Language: ENGLISH

Searcher : Shears 308-4994

BIOSIS COPYRIGHT: BIOL ABS. A prospective study was performed to evaluate the presence of colonization factor antigens (CFAs) in enterotoxigenic *Escherichia coli* (ETEC) strains isolated from 1,211 children with diarrhea in Argentina. One hundred nine ETEC strains that were isolated from seven different laboratories in various regions of the country were tested for CFAs by using *monoclonal*** antibodies against *CFA***/*I*** and the *E. coli* surface antigens CS1, CS2, and CS3 of CFA/II and *CS4*** and CS5 of CFA/IV; a polyclonal antiserum against CS6 was used. The CFAs searched for were found in 52% of the ETEC strains: 23% of the strains carried *CFA***/*I***, 17% carried *CFA***/IV, and 12% carried CFA/II. All of the *CFA***/*I*** strains produced heat-stable enterotoxin, and several of them were of the prevalent serotypes O153:H45 and O78:H12. Among the 19 strains expressing CFA/IV, 16 expressed CS5 and CS6 and produced the heat-stable enterotoxin and most were of serotype O128:H21, the remaining 3 strains produced CS6 only. No ETEC strains expressing *CS4*** were found. Most (11 of 13) of the CFA/II-carrying ETEC strains expressed CS1 and CS3, and 10 of them were of the O6:K15:H16 serotype and produced both heat-labile and heat-stable toxins. As many as 24 of the 109 CFA-negative ETEC strains gave mannose-resistant hemagglutination with erythrocytes from different species; 4 strains had high surface hydrophobicity, suggesting the presence of additional, as yet undefined, colonization factors in up to 25% of the ETEC isolates.

5/3,AB/4 (Item 1 from file: 357)
 DIALOG(R)File 357:Derwent Biotechnology Abs
 (c) 2000 Derwent Publ Ltd. All rts. reserv.

0223661 DBA Accession No.: 98-05258 PATENT
 *Monoclonal*** antibody agglutinating *Escherichia coli* with *CS4***/*CFA***
 /*I*** family protein - produced by *hybridoma*** cell culture, used
 for infection diagnosis and diarrhea therapy
 AUTHOR: Cassels F; Lees A; Schuman R
 CORPORATE SOURCE: Fort Derrick, MD, USA; Rockville, MD, USA.
 PATENT ASSIGNEE: U.S.Army; Virion-Systems 1998
 PATENT NUMBER: WO 9805687 PATENT DATE: 980212 WPI ACCESSION NO.:
 98-145553 (9813)

PRIORITY APPLIC. NO.: US 23075 APPLIC. DATE: 960802
 NATIONAL APPLIC. NO.: WO 97US13477 APPLIC. DATE: 970801
 LANGUAGE: English

ABSTRACT: A new *monoclonal*** antibody (*Mab***) that binds exclusively to a defined protein sequence and agglutinates *Escherichia coli* bearing *CS4***/*CFA***/*I*** family protein, is produced by *hybridoma*** *96***-109FE8*** IH11. The *Mab*** may be used to detect enterotoxigenic *E. coli* by contacting cultures of the microorganism with the *Mab*** and detecting *Mab***/*CS4***-CFA***/*I*** protein binding complexes (claimed). The *Mab*** may also be included in compositions with a carrier appropriate for application to bacteria-containing growth media, optionally with a tag, e.g. a
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fluorescing agent or colometric tag to assist complex identification.

The new *Mab*** may be included in a composition with a pharmaceutically acceptable carrier, especially saline, for treating or prophylaxing against illness arising from infection with bacteria bearing the *CS4***-*CFA***/*I*** protein, such as diahorrea. (14pp)

5/3,AB/5 (Item 2 from file: 357)

DIALOG(R)File 357:Derwent Biotechnology Abs

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0143371 DBA Accession No.: 93-01423

Induction of *colonization*** *factor*** antigen-*I*** (*CFA***/*I***) and *coli*** *surface*** antigen-*4*** (*CS4***) of enterotoxigenic Escherichia coli: relevance for vaccine production - use of a cloned cfaD gene to restore and enhance the production of intact *CFA***/*I*** and *CS4*** pilus

AUTHOR: Grewal H M S; Gaastra W; Svennerholm A M; Roli J; Sommerfelt H
CORPORATE SOURCE: Centre for International Health, University of Bergen, Haukeland Hospital, N-5021 Bergen, Norway.

JOURNAL: Vaccine (11, 2, 221-26) 1993

CODEN: VACCDE

LANGUAGE: English

ABSTRACT: Regulatory proteins control the expression of the fimbrial *colonization*** *factor*** antigens (*CFA***/*I***) and *coli*** *surface*** antigen-*4*** (*CS4***) of enterotoxigenic Escherichia coli (ETEC). To examine the mechanism behind lack of expression of these antigens in spontaneous CFA-negative mutants, recombinant plasmid PIBV3-100 harboring the cfaD gene, which encodes a positive regulator of *CFA***/*I*** and *CS4*** expression, was mobilized into such derivatives. In electron microscopy, the induced surface structures were morphologically identical to the fimbriae of the *CFA***/*I***+ and *CS4***+ wild-type strains. Immunogold labeling with *monoclonal*** antibodies showed that the distribution of *CFA***/*I*** and *CS4*** specific epitopes along the induced fimbriae was indistinguishable from that of the wild-type strains. The percentage of fimbriated cells was higher in the cfaD transformants than in the wild-type strains. The efficiency of the cloned cfaD gene in restoring and enhancing the production of morphologically intact *CFA***/*I*** and *CS4*** fimbriae is reported. The technique may be useful in the large-scale production of whole cell and subunit ETEC vaccines. (35 ref)

5/3,AB/6 (Item 3 from file: 357)

DIALOG(R)File 357:Derwent Biotechnology Abs

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0131881 DBA Accession No.: 92-04373

Induction of *colonization*** *factor*** antigen *I***, *coli***

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*surface*** antigen *4*** and putative colonization factor antigen 0166
of enterotoxigenic Escherichia coli - pilus recombinant vaccine
construction (conference abstract)

AUTHOR: Grewal H M S; Gaastra W; Svennerholm A M; Sommerfelt H

CORPORATE SOURCE: CIH, University of Bergen, 5021 Norway.

JOURNAL: Vaccine (10, 4, 270) 1992

CODEN: VACCDE

LANGUAGE: English

ABSTRACT: The development of fimbrial (pilus) vaccines for enterotoxigenic Escherichia coli (ETEC) is complicated by the existence of a wide range of ETEC fimbriae. Plasmid DNA from 3 ETEC strains, negative in phenotypic assays for known fimbrial antigens, showed restriction fragment patterns characteristic of DNA associated with *colonization*** *factor*** antigen *I*** (*CFA***/*I***), *coli***- *surface*** antigen *4*** (*CS4***) and putative colonization factor 0166 (PCF0166). A plasmid encoding the positive *CFA***/*I*** regulator, CfaD, was mobilized into these strains, resulting in a high level of *CFA***/*I***, *CS4*** and PCF0166 production, respectively. Electron microscopy showed fimbriae morphologically identical to those present on wild-type ETEC producing *CFA***/*I***, *CS4*** and PCF0166. Immunogold labeling using *monoclonal*** antibodies against *CFA***/*I***, *CS4*** and PCF0166 revealed that the distribution of gold particles along the induced fimbriae was indistinguishable from that of corresponding wild-type strains. The induction of fimbrial expression by a common positive regulator may be instrumental in the production of vaccine strain(s) engineered to express several CFAs, to protect against a spectrum of ETEC. (0 ref)

5/3,AB/7 (Item 1 from file: 440)

DIALOG(R)File 440:Current Contents Search(R)

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11254296 GENUINE ARTICLE#: 273CN NUMBER OF REFERENCES: 27

TITLE: Prevalence of toxin types and colonization factors in
enterotoxigenic Escherichia coli isolated during a 2-year period from
diarrheal patients in Bangladesh

AUTHOR(S): Qadri F (REPRINT); Das SK; Faruque ASG; Fuchs GJ; Albert MJ;
Sack RB; Svennerholm AM

AUTHOR(S) E-MAIL: fqadri@icddrb.org

CORPORATE SOURCE: ICDDR B, Div Sci Lab, GPO Box 128/Dhaka 1000//Bangladesh/
(REPRINT); ICDDR B, Div Sci Lab, /Dhaka 1000//Bangladesh/; Johns
Hopkins Univ, Dept Int Hlth, /Baltimore//MD/; Gothenburg Univ, Dept Med
Microbiol & Immunol, /S-41346 Gothenburg//Sweden/

PUBLICATION TYPE: JOURNAL

PUBLICATION: JOURNAL OF CLINICAL MICROBIOLOGY, 2000, V38, N1 (JAN), P27-31

PUBLISHER: AMER SOC MICROBIOLOGY, 1325 MASSACHUSETTS AVENUE, NW,
WASHINGTON, DC 20005-4171 USA

ISSN: 0095-1137

Searcher : Shears 308-4994

LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: The prevalence of toxin types and colonization factors (CFs) of enterotoxigenic Escherichia coli (ETEC) was prospectively studied with fresh samples (n = 4,662) obtained from a 2% routine surveillance of diarrheal stool samples over 2 years, from September 1996 to August 1998. Stool samples were tested by enzyme-linked immunoassay techniques and with specific *monoclonal*** antibodies for the toxins and CFs. The prevalence of ETEC was 14% (n = 662), with over 70% of the strains isolated from children 0 to 5 years of age, of whom 93% were in the 0- to 3-year-old age range. Of the total ETEC isolates, 49.4% were positive for the heat-stable toxin (ST), 25.4%, were positive for the heat-labile toxin (LT) only, and 25.2% were positive for both LT and ST. The rate of ETEC isolation peaked in the hot summer months of May to September and decreased in winter. About 56% of the samples were positive for 1 or more of the 12 CFs that were screened for. The coli surface antigens *CS4***, CS5, and/or CS6 of the colonization factor antigen (CFA)ITV complex were most prevalent (incidence, 31%), followed by CPA/I (23.5%) and coli surface antigens CS1, CS2, and CS3 of CFA/II (21%). In addition, other CFs detected in decreasing order were CS7 (8%), CS14 (PCF0166) (7%), CS12 (PCF0159) (4%), CS17 (3%), and CS8 (CFA/III) (2.7%). The ST- or LT- and ST-positive ETEC isolates expressed the CFs known to be the most prevalent (*i***.e., *CFA***/*I***, *CFA***/II, and *CFA***/IV), while the strains positive for LT only did not. Among children who were infected with ETEC as the single pathogen, a trend of relatively more severe disease in children infected with ST-positive (P < 0.001) or LT- and ST-positive (P < 0.001) ETEC isolates compared to the severity of the disease in children infected with LT only-positive ETEC isolates was seen. This study supports the fact that ETEC is still a major cause of childhood diarrhea in Bangladesh, especially in children up to 3 years of age, and that measures to prevent such infections are needed in developing countries.

ISSN: 0095-1137

5/3,AB/8 (Item 2 from file: 440)

DIALOG(R)File 440:Current Contents Search(R)

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10138548 GENUINE ARTICLE#: 151MW NUMBER OF REFERENCES: 38

TITLE: Oral, inactivated, whole cell enterotoxigenic Escherichia coli plus cholera toxin B subunit vaccine: Results of the initial evaluation in children

AUTHOR(S): Savarino SJ (REPRINT); Hall ER; Bassily S; Brown FM; Youssef F; Wierzbza TF; Peruski L; El-Masry NA; Safwat M; Rao M; El Mohamady H; Abu-Elyazeed R; Naficy A; Svennerholm AM; Jertborn M; Lee YJ; Clemens JD

AUTHOR(S) E-MAIL: savarino@namru3.navy.mil

CORPORATE AUTHOR(S): PRIDE Study Grp

Searcher : Shears 308-4994

08/905046

CORPORATE SOURCE: USN, Med Res Unit 3, PSC 452, Box 5000/FPO//AE/09835
(REPRINT); USN, Med Res Unit 3, /Cairo//Egypt/; Egyptian Minist Hlth,
/Benha//Egypt/; Qalyubia Governorate, /Governorate//Egypt/; NICHHD,
NIH, /Bethesda//MD/20892; Gothenburg Univ, Dept Med Microbiol &
Immunol, /S-41124 Gothenburg//Sweden/

PUBLICATION TYPE: JOURNAL

PUBLICATION: JOURNAL OF INFECTIOUS DISEASES, 1999, V179, N1 (JAN), P107-114

PUBLISHER: UNIV CHICAGO PRESS, 5801 S ELLIS AVENUE, CHICAGO, IL 60637 USA

ISSN: 0022-1899

LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: Two randomized, double-blinded trials assessed the safety and immunogenicity of an oral, killed enterotoxigenic Escherichia coli (ETEC) plus cholera toxin B subunit vaccine in Egyptian children. Two doses of vaccine or E. coli K-12 were given 2 weeks apart to 105 6- to 12-year-olds and 97 2- to 5-year-olds. Safety was monitored for 3 days after each dose. Blood was collected before immunization and 7 days after each dose to measure immune responses. Few children reported postdosing symptoms, with no differences in the frequency of symptoms between treatment groups. Most vaccinees had an IgA antibody-secreting cell response against *colonization*** *factor*** antigen *I*** (100%, 6-12 years; 95%, 2-5 years), coli surface antigen 2 (92%, 6-12 years; 83%, 2-5 years), and *coli*** *surface*** antigen *4*** (93%, 6-12 years). Vaccination evoked a greater than or equal to 4-fold rise in antitoxic IgA and IgG titers in 93% and 81% of children, respectively. In conclusion, the oral ETEC vaccine was safe and immunogenic in 2- to 12-year-old children, justifying further evaluation in infants.

ISSN: 0022-1899

5/3,AB/9 (Item 3 from file: 440)

DIALOG(R) File 440:Current Contents Search(R)

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09080432 GENUINE ARTICLE#: YN990 NUMBER OF REFERENCES: 11

TITLE: Infection with *colonization*** *factor*** antigen *I***-expressing enterotoxigenic Escherichia coli boosts antibody responses against heterologous colonization factors in primed subjects

AUTHOR(S): Rudin A (REPRINT); Wiklund G; Wenneras C; Qadri F

CORPORATE SOURCE: GOTHENBURG UNIV, DEPT MED MICROBIOL & IMMUNOL,
GULDHEDSGATAN 10A/S-41346 GOTHENBURG//SWEDEN/ (REPRINT); INT CTR
DIARRHOEAL DIS RES, /DHAKA//BANGLADESH/

PUBLICATION TYPE: JOURNAL

PUBLICATION: EPIDEMIOLOGY AND INFECTION, 1997, V119, N3 (DEC), P391-393

PUBLISHER: CAMBRIDGE UNIV PRESS, 40 WEST 20TH STREET, NEW YORK, NY

10011-4211

ISSN: 0950-2688

LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: Enterotoxigenic Escherichia coli (ETEC) adhere to the intestinal mucosa by a number of fimbrial colonization factors (CFs) that have

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been claimed to induce only type-specific immunity. However, adult Bangladeshi patients infected with *CFA***/*I***-expressing bacteria, developed significant plasma IgA antibody responses, as determined by enzyme-linked immunosorbent assay, not only against the homologous fimbriae but also against several heterologous CFs, i.e. CS1, CS2, *CS4*** and PCF0166 fimbriae. In contrast, North American volunteers, who had probably not been infected by ETEC previously, responded with serum IgA against *CFA***/*I*** fimbriae but not against any other CFs after symptomatic infection with *CFA***/*I***-expressing ETEC. Thus, infection with *CFA***/*I***-expressing bacteria may boost immune responses against CFs with a related amino acid sequence in previously primed subjects.

ISSN: 0950-2688

5/3,AB/10 (Item 4 from file: 440)
 DIALOG(R)File 440:Current Contents Search(R)
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08141348 GENUINE ARTICLE#: WE900 NUMBER OF REFERENCES: 54

TITLE: A new putative fimbrial colonization factor, CS19, of human enterotoxigenic Escherichia coli

AUTHOR(S): Grewal HMS; Valvatne H; Bhan MK; vanDijk L; Gastra W; Sommerfelt H (REPRINT)

CORPORATE SOURCE: UNIV BERGEN,CTR INT HLTH, ARMAUER HANSENS BLDG/N-5021 BERGEN//NORWAY/ (REPRINT); UNIV BERGEN,CTR INT HLTH/N-5021 BERGEN//NORWAY//; UNIV BERGEN,BIOTECHNOL LAB/N-5021 BERGEN//NORWAY//; UNIV BERGEN,DEPT MICROBIOL & IMMUNOL, GADES INST/N-5021 BERGEN//NORWAY//; ALL INDIA INST MED SCI,DEPT PEDIAT, DIV GASTROENTEROL & ENTER INFECT/NEW DELHI//INDIA//; UNIV UTRECHT,FAC VET MED, INST INFECT DIS & IMMUNOL/UTRECHT//NETHERLANDS/

PUBLICATION TYPE: JOURNAL

PUBLICATION: INFECTION AND IMMUNITY, 1997, V65, N2 (FEB), P507-513

PUBLISHER: AMER SOC MICROBIOLOGY, 1325 MASSACHUSETTS AVENUE, NW, WASHINGTON, DC 20005-4171

ISSN: 0019-9567

LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: A gene probe derived from the *colonization*** *factor*** antigen *I*** (*CFA***/*I***) operon cross-hybridized at very low stringency to plasmid DNA from coli surface antigen 17 (CS17)-producing enterotoxigenic Escherichia coli (ETEC) and from the ETEC strain F595C, which was negative for previously described CFAs, CSs, and putative colonization factors (PCFs). A 16-kDa protein was identified in sodium dodecyl sulfate-polyacrylamide gel electrophoresis of heat extracts prepared after growth of strain F595C at 37 degrees C on CFA agar containing bile salts. Transmission electron microscopy revealed bile salt- and temperature-dependent expression of fimbriae with a diameter of 7 nm. After transformation with a recombinant plasmid harboring the cfaR gene, which encodes a positive regulator of several CFAs, PCFs,

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and CSs, the 16-kDa protein was hyperexpressed. Polyclonal antibodies raised against this protein bound to the fimbriae and inhibited the adhesion of F595C bacteria to tissue-cultured Caco-2 cells. Nucleotide sequence determination of the gene encoding the 16-kDa fimbrial subunit revealed a high degree of amino acid sequence homology to the *CFA***/*I***, CS1, CS2, *CS4***, CS14, and CS17 polypeptides. The term CS19 is proposed for the new fimbria.

ISSN: 0019-9567

5/3,AB/11 (Item 5 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)
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07551011 GENUINE ARTICLE#: UW559 NUMBER OF REFERENCES: 35
TITLE: *MONOCLONAL*** ANTIBODIES AGAINST FIMBRIAL SUBUNITS OF
*COLONIZATION*** *FACTOR*** ANTIGEN *I*** (*CFA***/*I***) INHIBIT
BINDING TO HUMAN ENTEROCYTES AND PROTECT AGAINST ENTEROTOXIGENIC
ESCHERICHIA COLI EXPRESSING HETEROLOGOUS COLONIZATION FACTORS
AUTHOR(S): RUDIN A; OLBE L; SVENNERHOLM AM (Reprint)
CORPORATE SOURCE: GOTHENBURG UNIV,DEPT MED MICROBIOL &
IMMUNOL,GULDHEDSGATAN 10A/S-41346 GOTHENBURG//SWEDEN/ (Reprint);
GOTHENBURG UNIV,DEPT MED MICROBIOL & IMMUNOL/S-41346
GOTHENBURG//SWEDEN/; GOTHENBURG UNIV,DEPT SURG/S-41346
GOTHENBURG//SWEDEN/

PUBLICATION: MICROBIAL PATHOGENESIS, 1996, V21, N1 (JUL), P35-45
ISSN: 0882-4010

LANGUAGE: ENGLISH DOCUMENT TYPE: ARTICLE

ABSTRACT: Enterotoxigenic Escherichia coli (ETEC) bind to enterocytes in the small intestine by means of antigenically distinct colonization factors (CFs). By immunizing with isolated subunits of CPA/I fimbriae we have previously produced *monoclonal*** antibodies (*Mabs***) that cross-react immunologically in vitro with several CFs. Two of these *Mabs*** [S(subunit)-*CFA***/*I*** 17:8 and S-*CFA***/*I*** 5:6] were found to significantly inhibit the binding of ETEC strains expressing either homologous or heterologous CFs, *i***.e. *CFA***/*I*** and *CS4***, to isolated human jejunal enterocytes. The two *Mabs*** also conferred passive protection against fluid accumulation in rabbit ileal loops caused by *CFA***/*I***- as well as *CS4***-expressing ETEC strains. Immunoelectron microscopy studies showed that both *Mabs*** bound specifically to *CFA***/*I*** as well as to *CS4*** fimbriae expressed on bacteria. These results indicate the possibility to induce anti-CF antibodies that can protect against ETEC infection caused by bacteria expressing not only homologous but also heterologous CFs, by immunizing with fimbrial subunits. (C) 1996 Academic Press Limited

ISSN: 0882-4010

5/3,AB/12 (Item 6 from file: 440)
Searcher : Shears 308-4994

DIALOG(R)File 440:Current Contents Search(R)
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05434528 GENUINE ARTICLE#: NM112 NUMBER OF REFERENCES: 31
TITLE: COLONIZATION FACTOR ANTIGENS (CFAS) OF ENTEROTOXIGENIC ESCHERICHIA
COLI CAN PRIME AND BOOST IMMUNE RESPONSES AGAINST HETEROLOGOUS CFAS
AUTHOR(S): RUDIN A; SVENNERHOLM AM (Reprint)
CORPORATE SOURCE: GOTHENBURG UNIV,DEPT MED MICROBIOL &
IMMUNOL,GULDHEDSGATAN 10 A/S-41346 GOTHENBURG//SWEDEN/ (Reprint);
GOTHENBURG UNIV,DEPT MED MICROBIOL & IMMUNOL/S-41346
GOTHENBURG//SWEDEN/
PUBLICATION: MICROBIAL PATHOGENESIS, 1994, V16, N2 (FEB), P131-139
ISSN: 0882-4010
LANGUAGE: ENGLISH DOCUMENT TYPE: ARTICLE
ISSN: 0882-4010

5/3,AB/13 (Item 7 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)
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03928579 GENUINE ARTICLE#: JJ861 NUMBER OF REFERENCES: 50
TITLE: GENETIC RELATIONSHIP OF PUTATIVE COLONIZATION FACTOR-0166 TO
*COLONIZATION*** *FACTOR*** ANTIGEN-*I*** AND *COLI*** *SURFACE***
ANTIGEN-*4*** OF ENTEROTOXIGENIC ESCHERICHIA-COLI
AUTHOR(S): SOMMERFELT H; GREWAL HMS; SVENNERHOLM AM; GAASTRA W; FLOOD PR;
VIBOUD G; BHAN MK
CORPORATE SOURCE: UNIV BERGEN,HAUKELAND HOSP,CTR INT HLTH/N-5021
BERGEN//NORWAY/ (Reprint); UNIV BERGEN,BERGEN HIGH TECHNOL CTR,CTR
BIOTECHNOL/N-5020 BERGEN//NORWAY/; UNIV BERGEN,INST ANAT/N-5009
BERGEN//NORWAY/; ALL INDIA INST MED SCI,DEPT PEDIAT,DIV GASTROENTEROL &
ENTER INFECT/NEW DELHI 110029//INDIA/; GOTHENBURG UNIV,DEPT MED
MICROBIOL & IMMUNOL/S-41346 GOTHENBURG//SWEDEN/; UNIV UTRECHT,FAC VET
MED,INST INFECT DIS & IMMUNOL/3508 TD UTRECHT//NETHERLANDS/
PUBLICATION: INFECTION AND IMMUNITY, 1992, V60, N9 (SEP), P3799-3806
ISSN: 0019-9567
LANGUAGE: ENGLISH DOCUMENT TYPE: ARTICLE
ABSTRACT: Plasmid DNA from two strains of enterotoxigenic Escherichia coli
harboring genes encoding *coli*** *surface*** antigen *4*** (*CS4***)
and from seven Indian enterotoxigenic E. coli isolates cross-hybridized
at low stringency but not at high stringency with two polynucleotide
probes derived from the *colonization*** *factor*** antigen *I*** (
*CFA***/*I***) operon. Low-stringency Southern blot hybridization of
PstI-digested plasmid DNA from the seven Indian isolates yielded
characteristic restriction fragment patterns, distinct from those of
*CS4***- and *CFA***/*I***-associated plasmid DNA. Two of the Indian
strains were transformed with a recombinant plasmid harboring the cfaD
gene, which encodes a positive regulator of *CFA***/*I*** and *CS4***
genes. The cfaD transformants produced large amounts of putative

Searcher : Shears 308-4994

colonization factor O166 (PCFO166) irrespective of whether the nutrient agar contained bile salts, a growth factor otherwise required for adequate PCFO166 expression. A considerable interstrain variation in the level of PCFO166 production could be explained by differences in the proportion of bacteria that were fimbriated, as visualized by electron microscopy. The N-terminal amino acid sequence of PCFO166 fimbrial protein showed a high degree of homology with the corresponding sequences of *CFA***/*I*** and *CS4***.

ISSN: 0019-9567

5/3,AB/14 (Item 8 from file: 440)
 DIALOG(R)File 440:Current Contents Search(R)
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03772467 GENUINE ARTICLE#: HZ759 NUMBER OF REFERENCES: 43

TITLE: USE OF NONRADIOACTIVE DNA HYBRIDIZATION FOR IDENTIFICATION OF ENTEROTOXIGENIC ESCHERICHIA-COLI HARBORING GENES FOR *COLONIZATION*** *FACTOR*** ANTIGEN-*I***, *COLI*** *SURFACE*** ANTIGEN-*4***, OR PUTATIVE COLONIZATION FACTOR-O166

AUTHOR(S): SOMMERFELT H; GREWAL HMS; GAASTRA W; SVENNERHOLM AM; BHAN MK
 CORPORATE SOURCE: UNIV BERGEN,HAUKELAND HOSP,CTR INT HLTH/N-5021
 BERGEN//NORWAY/ (Reprint); UNIV BERGEN,HAUKELAND HOSP,DEPT MED B/N-5021
 BERGEN//NORWAY/; UNIV BERGEN,CTR BIOTECHNOL/N-5020 BERGEN//NORWAY/;
 UNIV UTRECHT,FAC VET MED,INST INFECT DIS & IMMUNOL/3508 TD
 UTRECHT//NETHERLANDS/; GOTHENBURG UNIV,DEPT MED MICROBIOL &
 IMMUNOL/S-41346 GOTHENBURG//SWEDEN/; ALL INDIA INST MED SCI,DEPT
 PEDIAT,DIV GASTROENTEROL & ENTER INFECT/NEW DELHI 110029//INDIA/
 PUBLICATION: JOURNAL OF CLINICAL MICROBIOLOGY, 1992, V30, N7 (JUL), P
 1823-1828

LANGUAGE: ENGLISH DOCUMENT TYPE: ARTICLE

ABSTRACT: We developed an accurate nonradioactive colony hybridization assay (NCHA) using a digoxigenin-labeled polynucleotide probe and an antidigoxigenin alkaline phosphatase conjugate for the identification of enterotoxigenic Escherichia coli (ETEC) harboring genes for *colonization*** *factor*** antigen *I*** (*CFA***/*I***), *coli*** *surface*** antigen *4*** (*CS4***), or putative colonization factor O166 (PCFO166). In this 2-day assay, visual registration of color intensity could be used to distinguish between *CFA***/*I***-positive strains and strains with the genetic potential to express *CS4*** or PCFO166. A rapid NCHA was developed by which the results could be read visually 7 h and 45 min after inoculation of the bacteria. In the rapid NCHA, densitometry verified the visual discrimination between four groups of E. coli; ETEC with the *CFA***/*I*** gene, ETEC with the *CS4*** gene, ETEC with the PCFO 1 66 gene, and E. coli strains that lack such genes. As a confirmatory test, plasmids from ETEC with the *CFA***/*I***, *CS4***, or PCFO166 gene were differentiated by their characteristic restriction fragment patterns in nonradioactive Southern blot hybridization.

Searcher : Shears 308-4994

08/905046

5/3,AB/15 (Item 1 from file: 348)
DIALOG(R)File 348:European Patents
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00931498

ORDER fax of complete patent from Dialog SourceOne. See HELP ORDER 348
*MONOCLONAL*** ANTIBODY WHICH AGGLUTINATES E. COLI HAVING THE *CS4***-
*CFA***/I*** FAMILY PROTEIN
MONOKLONALER ANTIKORPER FUR DIE AGGLUTINIERUNG VON E. COLI, DAS EIN PROTEIN
DER *CS4***/CFA-FAMILIE ENTHALT
ANTICORPS *MONOCLONAL*** PERMETTANT D'AGGLUTINER E. COLI POSSEDANT UNE
PROTEINE DE LA FAMILLE *CS4***-CFA***/I***
PATENT ASSIGNEE:

DEPARTMENT OF THE ARMY, U.S. GOVERNMENT, (1745491), John Moran, Office of
Command Judge Adv., HQ USAMRDC, Departm. of the Army, Frederick, MD
21702-5012, (US), (applicant designated states:
AT;BE;CH;DE;DK;ES;FI;FR;GB;GR;IE;IT;LI;LU;MC;NL;PT;SE)
Virion Systems, Inc., (2429140), Suite 100, 9610 Medical Center Drive,
Rockville, MD 20850, (US), (applicant designated states:
AT;BE;CH;DE;DK;ES;FI;FR;GB;GR;IE;IT;LI;LU;MC;NL;PT;SE)

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SCHUMAN, Richard, 14317 Night Hawk Way, Gaithersburg, MD 20878, (US)

LEGAL REPRESENTATIVE:

Harding, Charles Thomas (70742), D. Young & Co. 21 New Fetter Lane,
London EC4A 1DA, (GB)

PATENT (CC, No, Kind, Date): EP 918796 A1 990602 (Basic)
WO 9805687 980212

APPLICATION (CC, No, Date): EP 97938077 970801; WO 97US13477 970801

PRIORITY (CC, No, Date): US 23075 P 960802

DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU;
MC; NL; PT; SE

INTERNATIONAL PATENT CLASS: C07K-016/12; C12N-005/12; G01N-033/569;
A61K-039/395;

NOTE:

No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English

5/3,AB/16 (Item 2 from file: 348)
DIALOG(R)File 348:European Patents
(c) 2000 European Patent Office. All rts. reserv.

00557311

ORDER fax of complete patent from Dialog SourceOne. See HELP ORDER 348
PREPARATION AND USE OF FORMALIN-KILLED COLONIZATION-FACTOR-ANTIGEN
Searcher : Shears 308-4994

08/905046

(CFA)-EXPRESSING E. COLI ORGANISMS FOR VACCINATION AGAINST ENTERIC INFECTION/DIARRHEA CAUSED

DARSTELLUNG UND VERWENDUNG VON MIT FORMALIN ABGETOTETEN E. COLI BAKTERIEN, DIE DAS KOLONIE-FAKTOR-ANTIGEN (CFA) EXPREMIEREN ZUR IMPFUNG GEGEN DAS DIE DARMINFEKT

PREPARATION ET UTILISATION D'ORGANISMES DE E. COLI TUES DANS LE FORMOL ET EXPRIMANT UN ANTIGENE DE FACTEUR DE COLONISATION (CFA) DANS LE BUT D'UNE VACCINATION C

PATENT ASSIGNEE:

Holmgren, Jan, (1145760), Korvettgatan 1D, S-421 74 Vastra Frolunda, (SE)
, (applicant designated states:

AT;BE;CH;DE;DK;ES;FR;GB;GR;IT;LI;LU;MC;NL;SE)

SVENNERHOLM, Ann-Mari, (1553120), Korvettgatan 1D, S-421 74 Vastra Frolunda, (SE), (applicant designated states:

AT;BE;CH;DE;DK;ES;FR;GB;GR;IT;LI;LU;MC;NL;SE)

INVENTOR:

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SVENNERHOLM, Ann-Mari, Korvettgatan 1D, S-421 74 Vastra Frolunda, (SE)

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PATENT (CC, No, Kind, Date): EP 573527 A1 931215 (Basic)

EP 573527 B1 980909

WO 9214487 920903

APPLICATION (CC, No, Date): EP 92906078 920225; WO 92SE110 920225

PRIORITY (CC, No, Date): SE 91556 910226

DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; LU; MC; NL;
SE

INTERNATIONAL PATENT CLASS: A61K-039/108;

NOTE:

No A-document published by EPO

LANGUAGE (Publication,Procedural,Application): English; English; English

FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	9837	281
CLAIMS B	(German)	9837	264
CLAIMS B	(French)	9837	321
SPEC B	(English)	9837	5891
Total word count - document A			0
Total word count - document B			6757
Total word count - documents A + B			6757

5/3,AB/17 (Item 1 from file: 35)

DIALOG(R)File 35:DISSERTATION ABSTRACTS ONLINE

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01531904 AADC527431

COLONISATION FACTORS OF ENTEROTOXIGENIC ESCHERICHIA COLI: CROSS-REACTIVE

Searcher : Shears 308-4994

AND PROTECTIVE EPITOPES (FIMBRIAL)

Author: RUDIN, ANNA

Degree: MED.DR

Year: 1996

Corporate Source/Institution: GOTEBORGS UNIVERSITET (SWEDEN) (0904)

Source: VOLUME 58/01-C OF DISSERTATION ABSTRACTS INTERNATIONAL.

PAGE 143. 63 PAGES

ISBN: 91-628-2044-3

Publisher: DEPT OF MEDICAL MICROBIOLOGY AND IMMUNOLOGY, GOTEBORG
UNIVERSITY, GULDHEDSGATAN 10, S-413 46 GOTEBORG, SWEDEN

Enterotoxigenic *Escherichia coli* (ETEC) is a main cause of diarrheal disease among children in developing countries and in travelers to these areas. ETEC express fimbrial colonisation factors (CFs), which enable binding of the bacteria to the intestinal mucosa and which are strong protective antigens. Hitherto, nineteen antigenically different CFs have been described. Although they are different, as determined by the reaction of anti-fimbrial antibodies in ELISA, the subunits of several of them, e.g., *CFA***/*I***, CS1, CS2, *CS4***, PCFO166 and CS17 fimbriae, have very significant amino acid sequence similarity. The aim of this thesis was to evaluate whether this sequence similarity might have any influence on anti-CF immune responses induced by immunisation or infection, and to identify cross-reactive B-cell epitopes that could give rise to cross-production.

By immunising mice with purified fimbriae and determining specific antibody titers as well as numbers of antibody producing cells, it was shown that *CFA***/*I*** could prime as well as boost the antibody response against *CS4***; similarly, *CS4*** could both prime and boost the response against *CFA***/*I***. Results analogous to these findings were found when analysing the serum antibody responses against CFs in groups of humans infected with *CFA***/*I***-expressing bacteria. Thus, Bangladeshi patients, who most likely had been repetitively primed with ETEC previously, responded not only against *CFA***/*I*** but also against several heterologous CFs, i.e. CS1, CS2, *CS4*** and PCFO166, whereas North American volunteers only responded against the homologous CF.

The *CFA***/*I*** fimbriae are composed of identical protein subunits in an helical arrangement. To expose potentially cross-reactive epitopes, purified *CFA***/*I*** fimbriae were dissociated into subunits and *monoclonal*** antibodies (*MAbs***) were raised against the subunits. *MAbs*** that cross-reacted with CS1, CS2, *CS4***, PCFO166 and CS17 were selected; two of these *MAbs***, *i***.e., S-*CFA***/*I*** 17:8 and S-*CFA***/*I*** 5:6, inhibited hemagglutination as well as binding to the enterocyte-like human Caco-2 cell-line of bacterial strains expressing homologous as well as antigenically different fimbriae. The two *MAbs*** were also shown to inhibit binding of bacteria expressing either *CFA***/*I*** or *CS4*** fimbriae to human jejunal epithelial cells as well as to confer passive protection against these strains in the rabbit ileal loop model. Immunoelectron microscopy analyses showed that the *MAbs*** bound to *CFA***/*I*** and *CS4*** fimbriae on bacteria.

Searcher : Shears 308-4994

By Pepscan analysis of the *Mab*** S-*CFA***/*I*** 17:8-specific epitope was determined to be linear and have the sequence \$\sp{15}\$IDLLQ\$\sp{19}\$. Immunisations of rabbits with an N-terminal 25 amino acid *CFA***/*I*** peptide, either coupled to a carrier protein or uncoupled, elicited strong anti-peptide as well as homologous and heterologous anti-fimbrial responses. The antisera did not inhibit binding of fimbriated ETEC to Caco-2 cells, which could be explained by Pepscan analysis showing that they did not bind to the epitope \$\sp{15}\$IDLLQ\$\sp{19}\$. Another peptide that could evoke antibodies against this epitope, or alternatively isolated *CFA***/*I*** subunits, might be interesting ETEC vaccine components.

5/3,AB/18 (Item 1 from file: 98)
DIALOG(R)File 98:General Sci Abs/Full-Text
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04032774 H.W. WILSON RECORD NUMBER: BGSA99032774
An outbreak of gastroenteritis in Japan due to Escherichia coli O166.
Nishikawa, Yoshikazu
Ogasawara, Jun; Helander, Anna
Emerging Infectious Diseases (Emerging Infect Dis) v. 5 no2 (Mar./Apr. 1999) p. 300
SPECIAL FEATURES: bibl ISSN: 1080-6040
LANGUAGE: English
COUNTRY OF PUBLICATION: United States
WORD COUNT: 693

ABSTRACT: An outbreak of gastroenteritis due to an EAST1-producing strain of Escherichia coli O166 is reported. EAST1 is the enteroaggregative E. coli heat stable enterotoxin 1. The gastroenteritis outbreak, which occurred on July 23, 1996, in Osaka, Japan, caused 54 of 91 persons attending a meeting held on the previous day to become ill. E. coli O166 with an unidentifiable H antigen was isolated from 29 of 33 stool specimens. Further analyses demonstrated that the causative agent of the outbreak was an EAST1-producing E. coli that did not have other well-characterized virulence genes. This isolate might form either a new group of diarrhea-associated E. coli or a new subgroup of enterotoxigenic E. coli..

? ds; t 15/3,ab/1-6; ds

Set	Items	Description
S6	64	AU=(CASSELS, F? OR CASSELS F?)
S7	1842	AU=(LEES, A? OR LEES A?)
S8	67	AU=(SCHUMAN, R? OR SCHUMAN R?)
S9	2	S6 AND S7 AND S8
S10	10	S6 AND (S7 OR S8)
S11	5	S7 AND S8
S12	1958	S6 OR S7 OR S8

Author (S)

Searcher : Shears 308-4994

08/905046

S13 5 S12 AND S3
S14 13 (S9 OR S10 OR S11 OR S13) NOT S4
S15 6 RD (unique items)
>>>No matching display code(s) found in file(s): 65, 113, 129, 130

15/3,AB/1 (Item 1 from file: 65)
DIALOG(R)File 65:Inside Conferences
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02192142 INSIDE CONFERENCE ITEM ID: CN022817484
Antibody to N-Terminal Consensus Is Cross-Reactive with All Six Members of
the Enterotoxigenic E. Coli CFA/I Family
*Cassels, F. J."**; *Lees, A."**; Hansen, B. D.; Barringer, J. D.
CONFERENCE: Cytokines, cholera and the gut-Joint meeting
P: 275-280
IOS, Ohmsha, 1995
ISBN: 905199298X; 4274901203
LANGUAGE: English DOCUMENT TYPE: Conference Papers
CONFERENCE EDITOR(S): Keusch, G. T.; Kawakami, M.
CONFERENCE SPONSOR: United States-Japan Cooperative Medical Sciences
 Program Panel on Malnutrition
 United States-Japan Cooperative Medical Sciences Program Panel
 on Cholera
CONFERENCE LOCATION: Kiawah Island, SC
CONFERENCE DATE: Nov 1995 (199511) (199511)

15/3,AB/2 (Item 2 from file: 65)
DIALOG(R)File 65:Inside Conferences
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01967841 INSIDE CONFERENCE ITEM ID: CN020496496
Linear epitopes of colonization factor antigen I and peptide vaccine
approach to enterotoxigenic Escherichia coli
*Cassels, F. J."**; Jarboe, D. L.; Reid, R. H.; *Lees, A."**
CONFERENCE: Peptide epitope mapping-Symposium
JOURNAL OF INDUSTRIAL MICROBIOLOGY AND BIOTECHNOLOGY, 1997; VOL 19;
NUMBER 1 P: 66-70
Stockton, 1997
ISSN: 1367-5435
LANGUAGE: English DOCUMENT TYPE: Conference Selected papers based on the
presentations at the symposium
CONFERENCE SPONSOR: Society for Industrial Microbiology
CONFERENCE LOCATION: Research Triangle Park, NC
CONFERENCE DATE: Aug 1996 (199608) (199608)

15/3,AB/3 (Item 1 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)
 Searcher : Shears 308-4994

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11245788 GENUINE ARTICLE#: 271NT NUMBER OF REFERENCES: 19

TITLE: Activation of soluble polysaccharides with

1-cyano-4-dimethylaminopyridinium tetrafluoroborate (CDAP) for use in protein-polysaccharide conjugate vaccines and immunological reagents.

II. Selective crosslinking of proteins to CDAP-activated polysaccharides

AUTHOR(S): Shafer DE; Toll B; *Schuman RF***; Nelson BL; Mond JJ; *Lees A (REPRINT)***

AUTHOR(S) E-MAIL: virion@radix.net

CORPORATE SOURCE: Virion Syst Inc, 9610 Med Ctr Dr/Rockville//MD/20850

(REPRINT); Virion Syst Inc, /Rockville//MD/20850; Uniformed Serv Univ Hlth Sci, /Bethesda//MD/20814

PUBLICATION TYPE: JOURNAL

PUBLICATION: VACCINE, 2000, V18, N13 (JAN 18), P1273-1281

PUBLISHER: ELSEVIER SCI LTD, THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, OXON, ENGLAND

ISSN: 0264-410X

LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: Covalently linking protein to polysaccharides converts the anti-polysaccharide immune response from a T-cell independent response to one which is T-cell dependent. The organic cyanylating reagent 1-cyano-4-dimethylaminopyridinium tetrafluoroborate (CDAP) (Vaccine 14:190, 1996) has been used to activate polysaccharides, which can then be reacted with spacer reagents or directly with protein. We wished to explore ways in which proteins could be linked to CDAP-activated polysaccharides to conjugate in a more controlled and selective fashion. To this end, we examined the reaction of nucleophilic amino acids with CDAP-activated polysaccharides under basic and acidic conditions. We found that lysine, cysteine and histidine but not methionine, serine or tyrosine conjugated to CDAP-activated dextran. We also examined the reaction of various spacer reagents with CDAP-activated dextran as a function of pH. The addition of hexanediamine was highly pH dependent and maximal at pH 9.3. In contrast, the addition of adipic dihydrazide, which has a pKa of ca 2.5 was essentially independent of pH. By performing the conjugation reaction at pH 5, we were able to selectively couple hydrazides even in the presence of high concentrations of amines. Proteins derivatized with limited numbers of hydrazides could be conjugated to CDAP-activated polysaccharides at pH5, where the native protein was not reactive. Proteins could be derivatized with hydrazides on carboxyls using adipic dihydrazide and a water soluble carbodiimide or on amines using a mild two-step reaction. Tetanus toxoid-pneumococcal type 14 conjugates produced by coupling hydrazide-derivatized tetanus toroid under acidic conditions induced anti-polysaccharide antibodies at titers comparable to that stimulated by conjugates produced using a basic coupling pH. Our data suggest that crosslinking was occurring only with the limited number of hydrazides on the protein and that we

Searcher : Shears 308-4994

achieved limited and selective crosslinking between the protein and CDAP-activated polysaccharide. This work also demonstrates that CDAP-mediated conjugation to polysaccharides can be applied even to very pH sensitive proteins and polysaccharides. Published by Elsevier Science Ltd.

ISSN: 0264-410X

15/3,AB/4 (Item 2 from file: 440)
 DIALOG(R)File 440:Current Contents Search(R)
 (c) 2000 Inst for Sci Info. All rts. reserv.

08878113 GENUINE ARTICLE#: BJ63E NUMBER OF REFERENCES: 0
 TITLE: Antibody to N-terminal consensus peptide is cross-reactive with all six members of the enterotoxigenic E-coli *CFA***/I*** family
 AUTHOR(S): *Cassels FJ (REPRINT)***; *Lees A***; Hansen BD; Barringer JD; Nelson BL; Ryu H; Keusch GT; Kawakami M
 CORPORATE SOURCE: WALTER REED ARMY MED CTR,WALTER REED ARMY INST RES, DEPT GASTROENTEROL/WASHINGTON//DC/20307 (REPRINT)
 PUBLICATION TYPE: BOOK
 PUBLICATION: CYTOKINES, CHOLERA, AND THE GUT, 1995, P275-279
 PUBLISHER: I O S PRESS, VAN DIEMENSTRAAT 94, 1013 CN AMSTERDAM, NETHERLANDS
 ISBN: 90-5199-298-X LIBRARY OF CONGRESS ID: 96-78112
 LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: The *CFA***/I*** family of enterotoxigenic Escherichia coli (ETEC) colonization factors (CF) consists of *CFA***/I***, CSI, CS2, *CS4***, CS17, and PCF O166. They have been grouped as a family due to protein sequence homology as well as immunologic cross-reactivity. In this study, additional protein sequence of CS2, *CS4***, CS17, and PCF O166 was obtained. From this sequence a consensus was derived, a thirty-six amino acid peptide corresponding to this consensus synthesized, the peptide conjugated to a carrier protein, and rabbits immunized. Sera tested positive in an immunoblot (Western) assay against the peptide as well as against each of the members of the *CFA***/I*** family. The sera also agglutinated ETEC strains bearing CSI, CS2, and *CFA***/I*** in a slide agglutination test. These data demonstrate that a peptide derived from the consensus of the N-terminus of the *CFA***/I*** family is immunogenic and cross-reactive to each member of the family. It is hoped that these and additional studies may lead to a cross-protective Vaccine to ETEC strains bearing these CF, as well as to a broadly reactive reagent useful in CF detection.

15/3,AB/5 (Item 1 from file: 348)
 DIALOG(R)File 348:European Patents
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00931261
 ORDER fax of complete patent from Dialog SourceOne. See HELP ORDER 348
 Searcher : Shears 308-4994

08/905046

PEPTIDES RESPONSIVE TO ANTIBODIES AGAINST A CONSENSUS PEPTIDE OF THE
*CS4***-CFA***/I*** FAMILY PROTEINS
PEPTIDE SPEZIFISCH FUR ANTIKORPER GEGEN PEPTIDCONCENSUSSEQUENZEN AUS DER
*CS4***-CFA/IPRPTEINFAMILIE
PEPTIDES SENSIBLES A DES ANTICORPS DIRIGES CONTRE UN PEPTIDE CONSENSUS DES
PROTEINES DE LA FAMILLE C54-CFA***/I***

PATENT ASSIGNEE:

U.S. DEPARTMENT OF THE ARMY, (1992481), Medical Research and development
Command, Fort Frederick, MD 21702-5012, (US), (Applicant designated
States: all)

INVENTOR:

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LEGAL REPRESENTATIVE:

Harding, Charles Thomas (70742), D. Young & Co. 21 New Fetter Lane,
London EC4A 1DA, (GB)

PATENT (CC, No, Kind, Date): EP 959895 A1 991201 (Basic)
WO 9805348 980212

APPLICATION (CC, No, Date): EP 97936322 970801; WO 97US13476 970801

PRIORITY (CC, No, Date): US 23076 P 960802; US 23145 P 960805

DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU;
MC; NL; PT; SE

INTERNATIONAL PATENT CLASS: A61K-038/00; A61K-039/395; C07K-002/00;
C07K-004/00; C07K-005/00; C07K-007/00; C07K-014/00; C07K-016/00;
C07K-017/00; C12P-021/08; G01N-033/53

NOTE:

No A-document published by EPO

LANGUAGE (Publication,Procedural,Application): English; English; English

15/3,AB/6 (Item 2 from file: 348)
DIALOG(R)File 348:European Patents
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00825570

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METHODS OF RAISING ANTIBODIES AGAINST E.COLI OF THE FAMILY *CS4***-CFA***/
*I***

VERFAHREN ZUR HERSTELLUNG VON ANTIKORPERN GEGEN E.COLI BAKTERIEN DER
FAMILIE CS4CFA/1

PROCEDE VISANT A DRESSER DES ANTICORPS CONTRE L'E. COLI DE LA FAMILLE
CS4CFA/1

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